

by Ozen et al include palpable purpura (mandatory) in the presence of one of the following: diffuse abdominal pain, any biopsy specimen showing predominant IgA deposition, arthritis or arthralgias, or renal involvement.⁶ Our patient had palpable purpura, and diffuse abdominal pain may have accompanied his other gastrointestinal symptoms (loose stools, decreased oral intake), but it is hard to definitively know because of the patient's age.

HSP has been observed in the setting of numerous infections and also after the administration of several vaccines, including those against influenza, pneumococcal disease, hepatitis B virus, and meningococcal disease. Reported cases have occurred in individuals aged 5 to 57 years; however, the dose sequence and type of vaccine are often not mentioned. Polysaccharide vaccines were reported in HSP cases after pneumococcal and meningococcal vaccination.^{2,4,8} The reported time course of symptom onset after vaccine administration ranges from 7 to 14 days. The most commonly reported symptoms include arthralgias, rashes, joint swelling, abdominal pain, and proteinuria.^{2-4,8} Our patient's time course of 14 days corresponds with previously reported cases of HSP after vaccination with similar organ systems affected.

In summary, we report the first case of HSP after the administration of the hepatitis A vaccine. It is possible that after administration of the hepatitis A vaccine, immune complexes may form between vaccine antigens and native antibodies, thereby initiating a vasculitic process.⁷ The temporal association between hepatitis A vaccination and the development of HSP in this patient is notable. This case report suggests that the hepatitis A vaccine has the potential to act as an inducing factor for HSP or perhaps another type of vasculitis. The role of meticulous history taking with special emphasis on vaccine history is imperative so that an appropriate diagnosis can be made early and management initiated. It has been suggested that children with a history of vaccine-induced vasculitis should not be revaccinated, but there are currently no clear guidelines for what is the most appropriate management.²

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SUCCESSFUL USE OF ECALLANTIDE TO TREAT A HEREDITARY ANGIOEDEMA ATTACK AFTER FAILURE OF C1 INHIBITOR PROPHYLAXIS

Hereditary angioedema (HAE) is an inherited disorder that results from absent or nonfunctional C1 esterase inhibitor.¹ In the United States, purified C1 inhibitor is approved, in different forms, for both prophylaxis and treatment of acute attacks of HAE.^{2,3} C1 inhibitor prevents HAE attacks by inhibiting the protease plasma kallikrein, preventing generation of bradykinin. In addition to C1 inhibitor, ecallantide, a novel plasma kallikrein inhibitor, is approved for the treatment of acute HAE attacks.⁴ We describe the case of a woman who received prophylactic C1 inhibitor for HAE before airway surgery but still had a postsurgical HAE attack, which responded to ecallantide.

A 49-year-old woman with known HAE had required 2 prior tracheostomies during laryngeal attacks that resulted in subglottic tracheal stenosis. She had mild dyspnea on exertion, resting stridor, and severe sleep apnea secondary to the tracheal stenosis. She was scheduled for outpatient tracheal dilation. Because C1 inhibitor is the only medication approved for prophylaxis of HAE attacks and the patient had been treated multiple times with ecallantide for acute HAE attack, the patient received 1,000 units of C1 inhibitor (Cinryze ViroPharma, Exton, Pennsylvania) for the first time on the morning of her surgery, with the plan to treat any subsequent attack with ecallantide. Approximately 2½ hours after receiving C1 inhibitor, she underwent the dilation procedure, in which she was not intubated but rather jet-ventilated through the laryngoscope and balloon. The surgery was performed without complications. She reported immediate relief of her obstructive symptoms and stridor.

While in the recovery room, 1½ hours after her procedure (4 hours after receiving C1 inhibitor), she developed submandibular neck swelling bilaterally that was firm, edematous, and tender to palpation, consistent with an HAE attack. She did not have shortness of breath, hives, other sites of angioedema, or vital sign changes. She was treated with ecallantide (Kalbitor Dyax, Cambridge, Massachusetts), 30 mg subcutaneously, and the angioedema almost completely resolved within 45 minutes. Although C1 inhibitor can take up to 4 hours to exert its effect in acute HAE attacks,⁵ it reaches peak plasma levels within 1 hour when used as prophylaxis,⁶ making it unlikely that our patient's improvement was due to the C1 inhibitor. Because of the patient's preference, she is not currently taking a prophylactic medication despite having frequent attacks.

The optimum treatment of HAE is rapidly evolving with the recent introduction of several new therapies and can be divided into long-term prophylaxis, short-term prophylaxis (eg, before dental procedures or surgery), and treatment of acute attacks. Attenuated androgens, such as danazol, have shown efficacy in many patients for long-term prophylaxis of HAE attacks, but adverse effects, including lipid abnormalities, virilization, increased liver enzymes, and, rarely, hepatic cysts and carcinomas, limit their use.⁷ Fibrino-

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lysis inhibitors, such as ϵ -aminocaproic acid, have also been used for prophylaxis, especially in children, but efficacy is limited.⁷ In addition, fibrinolysis inhibitors are associated with muscle pain, fatigue, and increased muscle enzyme levels in some patients.⁷ The approach to short-term prophylaxis is less well studied but has included intermittent use of androgens, C1 inhibitor replacement, and use of fresh frozen plasma. Two formulations of purified C1 inhibitor are now available in the United States. One (Cinryze) can be given intravenously 2 to 3 times per week for long-term prophylaxis, and another (Berinert CSL Behring, King of Prussia, Pennsylvania) is approved for acute attacks.^{2,3} Both formulations of C1 inhibitor were efficacious and well tolerated in trials, with rates of adverse events similar between C1 inhibitor and placebo.^{2,3} The plasma kallikrein antagonist ecallantide (Kalbitor) is also approved for treatment of acute attacks. It is given subcutaneously and because of its short half-life is not appropriate for long-term prophylaxis. Although ecallantide is generally well tolerated, it has been associated with episodes of hypersensitivity, including anaphylaxis,^{4,8} and is therefore only licensed for use under the supervision of a medical professional. Ecallantide also results in prolongation of the activated partial thromboplastin time, but bleeding is not an observed adverse effect.⁸

Although new therapies have significantly improved the treatment options for HAE patients, their optimal use is not clear. For example, it is not clear how a patient should be treated if prophylaxis does not work or if initial treatment of an acute HAE attack is unsuccessful. We demonstrate that ecallantide can be effective for the treatment of an acute HAE attack that occurred after short-term prophylaxis with C1 inhibitor. Ecallantide has a significantly greater affinity for plasma kallikrein than does C1 inhibitor,⁸ suggesting it might be preferred for treatment of attacks that occur while a patient is receiving C1 inhibitor prophylaxis, although this hypothesis needs to be tested in formal trials.

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